

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a *PNMT* nucleic acid sequence, wherein said nucleic acid molecule is at least ten nucleotides in length, and wherein said *PNMT* nucleic acid sequence comprises a nucleotide sequence variant at a position selected from the group consisting of:
 - a) position 32, 159, 298, 340, or 462 of SEQ ID NO:6;
 - b) position 1, 360, 616, or 757 relative to the guanine in the splice donor site of intron 1 within SEQ ID NO:1;
 - c) position 940 or 941 relative to the adenine in the *PNMT* translation initiation codon within SEQ ID NO:1; and
 - d) position -591, -392, -390, -229, or -184 relative to the adenine in the *PNMT* translation initiation codon within SEQ ID NO:1.
2. The isolated nucleic acid of claim 1, wherein said nucleotide sequence variant is a nucleotide substitution.
3. The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence variant is a thymine substitution for cytosine at position 940 relative to the adenine in the *PNMT* translation initiation codon, or an adenine substitution for guanine at position 941 relative to the adenine in the *PNMT* translation initiation codon.
4. The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence variant is a thymine substitution for guanine at position 1 relative to the guanine in the splice donor site of intron 1, a cytosine substitution for thymine at position 360 relative to the guanine in the splice donor site of intron 1, an adenine substitution for guanine at position 616 relative to the guanine in the splice donor site of intron 1, or an adenine substitution for cytosine at position 757 relative to the guanine in the splice donor site of intron 1.
5. The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence variant is a thymine substitution for guanine at position -591 relative to the adenine in the *PNMT* translation initiation codon within SEQ ID NO:1, a cytosine substitution for guanine at position -392 relative to the adenine in the *PNMT* translation initiation codon within SEQ

ID NO:1, an adenine substitution for guanine at position -390 relative to the adenine in the *PNMT* translation initiation codon within SEQ ID NO:1, an adenine substitution for guanine at position -229 relative to the adenine in the *PNMT* translation initiation codon within SEQ ID NO:1, or an adenine substitution for guanine at position -184 relative to the adenine in the *PNMT* translation initiation codon within SEQ ID NO:1.

6. The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence variant at position 32 of SEQ ID NO:6 is a guanine substitution for adenine.

7. The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence variant at position 159 of SEQ ID NO:6 is a thymine substitution for cytosine.

8. The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence variant at position 298 of SEQ ID NO:6 is a guanine substitution for adenine.

9. The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence variant at position 340 of SEQ ID NO:6 is a thymine substitution for cytosine.

10. The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence variant at position 462 of SEQ ID NO:6 is a guanine substitution for adenine.

11. An isolated nucleic acid encoding a *PNMT* polypeptide, wherein said polypeptide comprises a *PNMT* amino acid sequence variant relative to the amino acid sequence of SEQ ID NO:8, and wherein said amino acid sequence variant is at a residue selected from the group consisting of 9, 98, and 112.

12. The isolated nucleic acid of claim 11, wherein said amino acid sequence variant is a serine at residue 9, an alanine at residue 98, or a cysteine at residue 112.

13. An isolated *PNMT* polypeptide, wherein said polypeptide comprises a *PNMT* amino acid sequence variant relative to the amino acid sequence of SEQ ID NO:8, wherein said amino acid sequence variant is at a residue selected from the group consisting of 9, 98, and 112.

14. The isolated polypeptide of claim 13, wherein said amino acid sequence variant is a serine at residue 9, an alanine at residue 98, or a cysteine at residue 112.

15. The isolated polypeptide of claim 13, wherein activity of said polypeptide is altered relative to a wild type PNMT polypeptide.

16. An isolated nucleic acid molecule comprising a *PNMT* nucleic acid sequence, wherein said nucleic acid molecule is at least ten nucleotides in length, wherein said *PNMT* nucleic acid sequence has at least 99% sequence identity to a region of SEQ ID NO:6, wherein said *PNMT* nucleic acid sequence comprises a guanine at position 32, a thymine at position 159, a guanine at position 298, a thymine at position 340, or a guanine at position 462, and wherein said region is selected from the group consisting of:

- a) nucleotides 1 of 100 of SEQ ID NO:6;
- b) nucleotides 100 to 200 of SEQ ID NO:6;
- c) nucleotides 250 to 350 of SEQ ID NO:6;
- d) nucleotides 300 to 375 of SEQ ID NO:6; and
- e) nucleotides 420 to 500 of SEQ ID NO:6.

17. A method for determining if a subject is predisposed to a disease, wherein said method comprises:

- a) obtaining a biological sample from said mammal, and
- b) detecting the presence or absence of a *PNMT* nucleotide sequence variant in said sample, wherein predisposition to said disease is determined based on the presence or absence of said variant.

18. The method of claim 17, wherein said method further comprises detecting the presence or absence of a plurality of said *PNMT* nucleotide sequence variants in said sample to obtain a variant profile of said subject, and wherein predisposition to said disease is determined based on said variant profile.

19. The method of claim 18, wherein said disease is a multiple sclerosis.

20. The method of claim 18, wherein said disease is early onset Alzheimer's disease.

21. A method for assisting a medical or research professional, wherein said method comprises:

- a) obtaining a biological sample from a subject, and
- b) detecting the presence or absence of a plurality of *PNMT* nucleotide sequence variants in said sample to obtain a variant profile of said subject.

22. The method of claim 21, wherein said method further comprises communicating said profile to said medical or research professional.

23. A method for determining the methyltransferase status of an individual, said method comprising determining whether said subject comprises a variant *PNMT* nucleic acid.

24. A method for predicting the therapeutic efficacy of a compound in a subject, wherein metabolism of said compound comprises methylation, said method comprising:

- a) determining the methyltransferase status of said subject; and
- b) correlating said methyltransferase status with the ability of said subject to metabolize said compound, wherein said compound is predicted to be therapeutically effective if said methyltransferase status is enhanced in said subject, and wherein said compound is predicted not to be therapeutically effective if said methyltransferase status is reduced in said subject.

25. The method of claim 24, wherein said determining of said methyltransferase status comprises determining whether said subject comprises a variant *PNMT* nucleic acid.

26. The method of claim 25, wherein said variant *PNMT* nucleic acid comprises a non-synonymous single nucleotide polymorphism.

27. The method of claim 24, wherein said determining of said methyltransferase status comprises measuring methyltransferase activity in a biological sample from said subject.

28. The method of claim 27, wherein said methyltransferase activity is *PNMT* activity.

29. A method for predicting the therapeutic efficacy of a compound in a subject, wherein metabolism of said compound comprises methylation, said method comprising:

- a) estimating the level of methyltransferase activity in said subject; and

b) correlating said level of methyltransferase activity with the ability of said subject to metabolize said compound, wherein said compound is predicted to be therapeutically effective if said level of methyltransferase activity is increased in said subject, and wherein said compound is predicted not to be therapeutically effective if said level of methyltransferase activity is reduced in said subject.

30. The method of claim 29, wherein said methyltransferase is PNMT.

31. The method of claim 30, wherein said methyltransferase activity is estimated *in vitro* in a biological sample from said subject.

32. The method of claim 29, wherein said level of methyltransferase activity in said subject is estimated by determining whether said subject comprises a variant *PNMT* nucleic acid.

33. The method of claim 32, wherein said variant *PNMT* nucleic acid comprises a non-synonymous single nucleotide polymorphism.

34. A method for estimating the dose of a compound for administration to a subject, wherein metabolism of said compound comprises methylation, said method comprising determining the level of methyltransferase activity in a biological sample from said subject, wherein said dose is estimated to be higher if said level of methyltransferase activity is increased in said biological sample as compared to a control level of methyltransferase activity, and wherein said dose is estimated to be lower if said level of methyltransferase activity is decreased in said biological sample as compared to said control level of methyltransferase activity.

35. The method of claim 34, wherein said methyltransferase activity is PNMT activity.

36. The method of claim 34, wherein said determining of said level of methyltransferase activity comprises determining whether said subject comprises a variant *PNMT* nucleic acid.

37. The method of claim 36, wherein said variant *PNMT* nucleic acid comprises a non-synonymous single nucleotide polymorphism.